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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

ART UNIT	PAPER NUMBER
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DATE MAILED:

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/359,181

Applicant(s)

GRASSY ET AL.

Examiner

Mary K Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-73 is/are pending in the application.
- 4a) Of the above claim(s) 3, 6, 7, 11-17, 21-68 and 70-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4, 5, 8-10, 18-20 and 69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's election with traverse of Group I and immunomodulators in Paper No. 10 and 13 is acknowledged. The traversal is on the ground(s) that the restriction is improper between groups I-III, as the differing methods are interrelated, and that groups drawn to identified compounds, pharmaceuticals and methods of making pharmaceuticals are linked to the methods of groups I-III. This is not found persuasive because each separated method has differing steps, and goals, and differing results could be obtained from the practice of each method. The arguments in regard to the pharmaceuticals are not persuasive for the reasons set forth in the restriction requirement. They represent independent and distinct inventive categories, and would require extensive search and examination not required for the search of any other group.

The requirement is still deemed proper and is therefore made FINAL.

In response to the restriction requirement, Applicant reassorted the dependency of numerous claims from differing groups in order to force their examination with group I. Claims were also added, without any specific indication as to which group they are directed towards. This results in the following group of claims: Group I, claims 1, 2, 4, 5, 8-10, 12-20, 65-69. All other claims are drawn to non-elected groups.

Claims 3, 6, 7, 11, 20-64 and 70-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10 and 13.

Within Group I, Claims 12-17, and 65-68 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10 and 13.

Claims 1, 2, 4, 5, 8-10, 18-20 and 69 are under examination in this application.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 30 December 1997, and an application filed in France on 29 December 1998. It is noted, however, that applicant has not filed a certified copy of the priority application or the

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PCT application as required by 35 U.S.C. 119(b). This application is a continuation-in-part of a PCT application, and not a national stage application. In these situations, the International Bureau does **not** provide copies of the PCT application or the priority document. Certified copies must be submitted according to 35 USC 119(b) to obtain the priority benefits of those applications.

Specification

The specification is objected to as it fails to meet the requirements of the Sequence Rules. The Table at page 30 lists numerous peptide sequences which are lacking a sequence identifier, (SEQ ID NO: X) as required. See also page 31.

37 CFR 1.821 (d) states: Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims of the patent application.

Claim Objections

Claims 1, 2, 4, 5, 8-10, 18-20 and 69 are objected to because of the following informalities: the term "employing" in claim 1 is not standard US practice. The term "comprising" would be acceptable. The term "modelling" in claim 1 (and other claims) is a misspelling, "modeling" would be correct. It is recommended that Applicant also amend the claims to use American spellings, for example, of the word "behavior". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 5, 8-10, 18-20 and 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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The claims as a whole are vague and indefinite as to the particular methods being claimed. There is no clear interrelationship between the listed steps, nor is there adequate description of the method steps themselves. For example "a molecular modeling step" does not set forth how the modeling is to be done; by modeling the 3-D structure? Or the 2-D structure? The topology? The physiochemical activity? A biological activity? By prediction or modeling of the reactions a molecule participates in? Modeling the binding sites of a molecule? Similarly, the "combinatorial library binding step" covers a myriad of potential steps and types of library. It is unclear what order the steps of claim 1 should be implemented, and where, in these steps, that the filtering step should be performed. Using the "including" language does not necessarily imply that the steps must be performed in the recited order, but just that somewhere within the identification of desired molecules, each of these things take place.

In claims 1, 2, 18, the metes and bounds of the term "provision" are unclear. How does the computer-aided methods "provide" anything? The method can identify or describe, but does not actually provide a tangible element. Similarly the metes and bounds of the phrase "exhibiting a desired behavior" are unclear. A molecule can have an activity or property, but does not exhibit a behavior. Also, the phrase could imply that *in vitro*/*in vivo* studies are done (outside of the computer) to positively identify that the selected molecules actually have that activity. No such step is set forth.

It is unclear where the limitations of claims 2, 4, 5 and 8-10 should be added to the method of claim 1.

In claim 4, the phrase "method for designing molecules according to claim 1" is incorrect. Claim 1 is identified as a method for the provision, identification and description of molecules, and not design.

Further in claim 4, the metes and bounds of the phrase "on the basis of enrichment in molecular diversity terms" are completely unclear. What are molecular diversity terms? How does one "enrich" for them, and yet screen them at the same time. No concrete method step is set forth in the limitation such that its meaning is made clear.

The entirety of claim 5 lacks antecedent basis in claim 1, from which it was amended to depend. Claim 1 does not set forth any "criteria" such that "said criteria" is proper, nor does the

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phrase "is based on a non-linear function of a descriptor value" have any clear connection to the steps of claim 1.

Claims 8 and 9 recite "a candidate molecule" which is not included or described in claim 2 from which they have been amended to depend. No specific candidate molecules are set forth in claim 1.

Claim 10 is vague and indefinite as it refers to Table II in the body of the claim. MPEP 2173.05(s) states: Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted). Reference characters corresponding to elements recited in the detailed description and the drawings may be used in conjunction with the recitation of the same element or group of elements in the claims. See MPEP Section 608.01(m)(m).

In claim 18, line 5, the phrase "the candidate molecules" lacks antecedent basis in the claim. Claim 18 does not recite "candidate molecules."

The limitations of claim 69 are unclear. Whether or not a molecule has a certain activity does not require particular constraints. The conformational constraints can help *predict* whether a molecule is likely to have an immunomodulatory effect, but that prediction needs actual testing. Further, if one already knows that a particular conformation absolutely defines a particular property, then the method is unnecessary.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 4, 5, 8-10, 18-20 and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Krieger (February, 1996).

The claims are drawn to methods of selecting molecules having particular properties including a modeling step, a combinatorial library building step, and a filtering step or selection step. Filters can be static, (unchanging) or dynamic (changing under certain situations).

Krieger (Chemical and Engineering News, (12 February 1996) Vol. 74, No. 7, pages 67-73) disclose methods of selecting desired compounds using a variety of methods, and method steps including: a library building step (p67 col 3), a modeling step (the virtual library in virtual space (p68), comparing and filtering against databases, or for particular properties (p68). QSAR modeling can also be performed (p69). The reference further discloses a collection of software that comprises combinatorial chemistry software applications, molecular modeling software, and a data access and management application which allows filtering of data by various means and descriptors. The C2-diversity product provides for combinatorial library building, and selection based on various 2-D and 3-D descriptors for QSAR methods of identifying particular compounds with various potential properties. As such this publication meets the limitations of the above rejected claims.

Claims 1, 2, 4, 5, 8-10, 18-20 and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Krieger (September, 1996).

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Krieger (Chemical and Engineering News, (16 September, 1996) Vol. 74, No. 38, pages 30-37) discloses a variety of software modules for bioinformatics and computational chemistry. For example, Molecular Inventor allows for 3-D modeling and annotation, which can be linked to a database with sequence and activity information, and a combinatorial chemistry module. These modules (and many of the others disclosed) can be used to identify molecules meeting particular descriptors (filtered) which could have a desired activity. Therefore this disclosure meets the limitations of the above rejected claims.

Claims 1, 2, 4, 5, 8-10, 18-20 and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrafiotis et al. (US 5,463,564).

Agrafiotis et al (US 5,463,564, 31 October 1995) disclose methods for identifying molecules having a desired activity, including bioactive molecules such as peptides or small molecules. Agrafiotis et al describe and claim a computer-implemented method as follows: first, a directed combinatorial chemical library is created, next the structures of the compounds made are modeled and activities are determined. The data about these structures and activities are used to screen out compounds that are unsuitable, and to further refine the next round of library building. Therefore, this patent meets the limitations of the above rejected claims.

Claims 1, 2, 4, 5, 8-10, 18-20 and 69 are rejected under 35 U.S.C. 102(e) as being anticipated by Cramer et al. (US Patent 6,240,374).

Cramer et al. (US Patent 6,240,374) disclose computer-implemented methods for creating and modeling a virtual library, screening with a number of various descriptors, and selecting compounds having a particular property. Immunomodulators are specifically contemplated, as illustrated in Table 2 which lists anti-inflammatories, anti-asthmatics, and anti-anaphylactics all of which modulate the immune system. Cramer details a number of descriptors, which can range from 3-D information, to activity, to size, weight, etc. As such, Cramer anticipates the claimed invention.

Claims 1, 2, 4, 5, 8-10, 18-20 and 69 are rejected under 35 U.S.C. 102(e) as being anticipated by Cramer et al. (US Patent 6,185,506).

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Cramer et al. (US Patent 6,185,506) disclose computer-implemented methods for creating and modeling a virtual library, screening with a number of various descriptors, and selecting compounds having a particular property. Immunomodulators are specifically contemplated, as illustrated in Table 2 which lists anti-inflammatories, anti-asthmatics, and anti-anaphylactics all of which modulate the immune system. Cramer details a number of descriptors, which can range from 3-D information, to activity, to size, weight, etc. As such, Cramer anticipates the claimed invention.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Liang et al. US Patent 6,182,016 discloses molecular classification for property prediction.

Hruby et al. Biochem Journal (1990) Vol. 268 pages 249-262. Hruby et al. Discosemolecular design of receptor-selective peptide ligands..

Ajay et al. J Med. Chem. 1999, vol. 42 pages 4942-4951. Ajay discloses how to design libraries with CNS activity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can generally be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

Official fax numbers for this Art Unit are: (703) 308-4242, (703) 872-9306. An *unofficial* fax number, direct to the Examiner is (703) 746 5279. Please call prior to use of this number.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the TC1600 Receptionist whose telephone number is (703) 308-0196.

mkz
9/7/01

MARY K. ZEMAN
PATENT EXAMINER